REMARKS

Claims 454-575 were previously pending and under examination in this application. Claims 568-575 have been canceled hereinabove. Accordingly, claims 454-567 are presently pending in this application.

This paper follows a July 19, 2001 telephone conversation between Examiner Scott W. Houtteman, Group Art Unit 1656, and Applicants' undersigned attorney. During that conversation, Examiner Houtteman indicated that Applicants could proceed with filing an after final amendment to cancel claims 568-575, thereby materially reducing or simplifying the issues for appeal in this case.

With the cancellation of claims 568-575 above, the pending claims subject to Applicants' appeal are 454-567.

In view of the agreed cancellation of claims 568-575, which claims were drawn to a polymeric composition comprising phosphate moiety labeled nucleotides, Applicants have also requested that the title of their invention be changed. The new title, "Oligo- or Polynucleotides Comprising Phosphate-Moiety Labeled Nucleotides," is believed to be more descriptive of the subject matter set forth in the claims now pending, claims 454-567.

Entry of the new title and cancellation of claims 568-575 is respectfully requested.

* * * * * * *

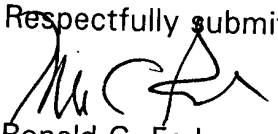
SUMMARY AND CONCLUSIONS

Claims 454-567 continue to be pending in this application with claims 568-575 having been canceled above by this paper.

No extension request or fee is believed due in connection with this filing, a Request For An Extension Of Time (3 Months) and authorization for the fee therefor having been filed with Applicants' January 18, 2001 Amendment Under 37 C.F.R. §1.116. No fee or fees are believed due in connection with this paper. In the event that any fee or fees are due, however, The Patent and Trademark Office is hereby authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,



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ATTACH #45

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July 16, 2001

BY HAND DELIVERY

Examiner Scott W. Houtteman
United States Patent & Trademark Office
Crystal Mall One
1911 South Clark Place Street
Arlington, VA 22202

Attention: **7th Floor Reception - Group Art Unit 1656**

Re: **U.S. Patent Application Serial No. 08/479,997**
Filed: **June 7, 1995**
Inventors: **Dean L. Englehardt et al.**
For: **OLIGO- OR POLYNUCLEOTIDES, AND OTHER COMPOSITIONS COMPRISING PHOSPHATE MOIETY LABELED NUCLEOTIDES**
Our Reference: Enz-5(D6)(C2)

Dear Examiner Houtteman:

This letter follows our July 9, 2001 interview and our July 11, 2001 Communication (To Provide Record Of The Substance Of The July 9, 2001 Interview).

One issue, the matter of claims 568-575, was unfortunately not addressed during our July 9th interview. These claims are drawn to a composition comprising a polymeric compound having at least one modified deoxyribonucleotide (claims 568-571) or modified ribonucleotide (claims 572-573) or modified nucleotide (claims 574-575). In an effort to materially reduce or simplify the issues for appeal, we had canceled claims 568-575 in our January 18, 2001 Amendment Under 37 C.F.R. §1.116. In the May 30, 2001 Advisory Action, you indicated that the proposed amendments will not be entered. Thus, claims 568-575 are still pending.

At this juncture, it would still be useful, particularly for purposes of appeal, to cancel claims 568-575. Such cancellation could be carried out either through an Examiner's Amendment or our own paper. Please let me know whether you wish to file an Examiner's Amendment or to have me file a paper to cancel the claims.

At the same time that I realized that claims 568-575 are still pending but should be canceled, I re-drafted the four independent claims (454, 482, 511 and 539). In so doing, I carefully considered your comments at the July 9th interview, the May 30, 2001 Advisory Action, and the earlier interview last summer regarding the "probe" nature of the compositions being claimed in this application.

In reviewing the proposed independent claims which are attached as Exhibit A, you will note the absence of the two phrases "or a portion thereof" (with respect to the "nucleic acid of interest") and "directly or indirectly detected" (with respect to the detection of the non-radioactive label moiety SIG). The former phrase was discussed at the July 9th interview and the former was cited in the May 30th Advisory Action.

I also considered your remarks in the May 30th Advisory Action regarding claim 539 that "[i]t is unclear whether SIG can attach to x, y and z when x, y and z are H– or HO– groups or if the definition of x, y and z was meant to change if a SIG moiety is attached." In response, I should point out that in claim 539 SIG can be attached to x, y or z when x, y or z are phosphate. Further, x, y or z can also be H– or HO– when at least one of the other three groups is phosphate and has SIG attached.

In the event that the amendments to the four independent claims could now be entered, I have also attached a marked up version of the claims to this letter. The clean copy and the marked up versions are attached as Exhibits A and B, respectively. All other amendments effected by our January 18, 2001 Amendment would not be entered as indicated in the May 30th Advisory Action.

Please let me know further whether you are willing to enter the proposed amendments to claims 454, 482, 511 and 539 as set forth in Exhibits A and B, and further, whether you would like me to submit a paper to make those changes.

Thank you.

Cordially,

Ronald C. Fedus
Corporation and Patent Counsel

Enclosures

Engelhardt et al., U.S. Pat. Appl. Ser. No. 08/479,997

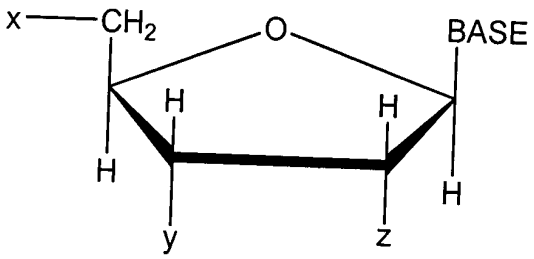
Clean Version of Replacement Claims 454, 482, 511 & 539

454. (Amended) An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the formula

Sig—PM—SM—BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig comprising a non-radioactive label moiety which can be detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest.

482. (Amended) An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1′ position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate; and

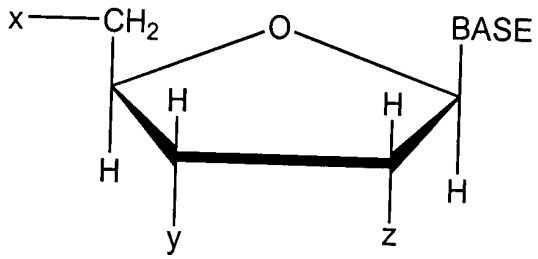
wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, said Sig comprising a non-radioactive label moiety which can be detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest.

511. (Amended) An oligo- or polyribonucleotide which is complementary to a nucleic acid of interest, said oligo- or polyribonucleotide comprising at least one modified ribonucleotide having the formula

Sig – PM – SM – BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM at a position of SM selected from the 2', 3' and 5' positions, or combinations thereof, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig comprising a non-radioactive label moiety which can be detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polyribonucleotide, or when said oligo- or polyribonucleotide is hybridized to said complementary nucleic acid of interest, provided that when Sig is attached through a chemical linkage to a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not a cleaved 3' terminal ribonucleotide previously attached to said oligo- or polyribonucleotide.

539. (Amended) An oligo- or polyribonucleotide which is complementary to a nucleic acid of interest, said oligo- or polyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, said Sig comprising a non-radioactive label moiety which can be detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polyribonucleotide, or when said oligo- or polyribonucleotide is hybridized to said complementary nucleic acid of interest, provided that when Sig is attached through a chemical linkage to y of a terminal ribonucleotide, said chemical linkage is not a cleaved 3' terminal ribonucleotide previously attached to said oligo- or polyribonucleotide.

* * * * * * *

Engelhardt et al., U.S. Pat. Appl. Ser. No. 08/479,997

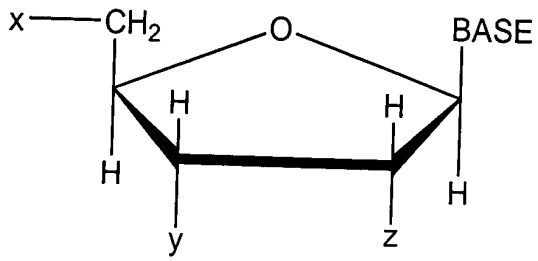
Version With Markings To Show Changes Made In Claims 454, 482, 511 & 539

454. (Amended) An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the formula

Sig—PM—SM—BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig [~~being a moiety capable of non-radioactive detection~~] comprising a non-radioactive label moiety which can be detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest.

482. (Amended) An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1′ position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate; and

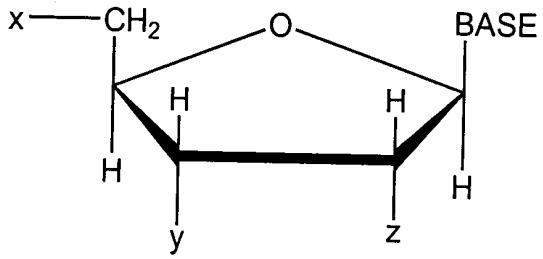
wherein Sig is covalently attached [~~to x, y or z~~] directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, said Sig [~~being a moiety capable of non-radioactive detection~~] comprising a non-radioactive label moiety which can be detected when so attached to [~~x, y or z~~] said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest.

511. (Amended) An oligo- or polyribonucleotide which is complementary to a nucleic acid of interest, said oligo- or polyribonucleotide comprising at least one modified ribonucleotide having the formula

Sig – PM – SM – BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM at a position of SM selected from the 2', 3' and 5' positions, or combinations thereof, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig [~~being a moiety capable of non-radioactive detection~~] comprising a non-radioactive label moiety which can be detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polyribonucleotide, or when said oligo- or polyribonucleotide is hybridized to said complementary nucleic acid of interest, provided that when Sig is attached through a chemical linkage to a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not a cleaved 3' terminal ribonucleotide previously attached to said oligo- or polyribonucleotide.

539. (Amended) An oligo- or polyribonucleotide which is complementary to a nucleic acid of interest, said oligo- or polyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached [~~to x, y or z~~] directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, said Sig [~~being a moiety capable of non-radioactive detection~~] comprising a non-radioactive label moiety which can be detected when so attached to [~~x, y or z~~] said phosphate or when said modified nucleotide is incorporated into said oligo- or polyribonucleotide, or when said oligo- or polyribonucleotide is hybridized to said complementary nucleic acid of interest, provided that when Sig is attached through a chemical linkage to y of a terminal ribonucleotide, said chemical linkage is not a cleaved 3' terminal ribonucleotide previously attached to said oligo- or polyribonucleotide.

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